

SUPPLEMENTAL TABLE S1 MICs ($\mu\text{g/ml}$) of antibiotics other than carbapenems, determined in absence and presence of two high NAC concentrations:

Enterobacteriaceae

Antibiotic	AMC			TZP			CTX			CRO			GEN			AMK			LVX			CST			
	NAC (mM)	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50
<i>E. coli</i> ATCC 25922	8	16	16	nd	nd	nd	0.06	0.125	0.06	0.06	0.06	0.25	0.25	1	1	1	1	2	2	≤ 0.03	≤ 0.03	≤ 0.03	0.5	0.5	0.5
<i>E. coli</i> Z21	64	64	64	nd	nd	nd	>512	>512	>512	>512	>512	>512	>512	2	4	4	16	32	32	64	64	32	1	0.5	0.5
<i>E. coli</i> Z24	8	8	8	nd	nd	nd	0.25	0.125	0.25	0.125	0.125	1	1	2	2	2	8	16	16	64	64	64	0.5	0.5	0.5
<i>E. coli</i> Z25	>64	64	>64	nd	nd	nd	>512	>512	>512	>512	>512	>512	>512	>256	>256	>256	32	32	64	16	16	16	1	0.5	0.5
<i>Kp</i> ATCC 700603	nd	nd	nd	16	16	8	4	8	4	4	8	8	8	16	16	16	1	2	2	1	0.5	1	1	1	1
<i>Kp</i> NTUH-K2044	nd	nd	nd	2	4	2	0.06	0.06	0.125	0.06	0.06	0.125	0.25	0.5	1	2	2	4	0.06	0.125	0.06	0.5	0.5	1	
<i>Kp</i> CIP 52.145	nd	nd	nd	2	2	2	0.06	0.06	0.06	0.06	0.06	0.25	0.25	0.5	1	1	2	4	0.06	0.06	0.06	0.5	0.5	1	
<i>Kp</i> Z4	nd	nd	nd	64	128	128	512	>512	512	>512	>512	>512	>256	>256	>256	>64	>64	>64	1	1	1	0.5	0.5	1	
<i>Kp</i> Z11	nd	nd	nd	>256	256	32	64	64	128	64	64	128	4	8	8	32	64	64	64	32	32	1	0.5	1	
<i>K. oxytoca</i> CCUG 15717 ^T	nd	nd	nd	4	4	4	0.06	0.06	0.06	0.125	0.25	0.25	1	2	1	2	4	4	0.06	0.06	0.06	0.5	0.5	0.5	
<i>E. cloacae</i> CIP 6085 ^T	nd	nd	nd	nd	nd	nd	8	8	4	8	4	16	0.5	1	1	1	2	2	≤ 0.03	≤ 0.03	≤ 0.03	64	64	64	
<i>E. cloacae</i> Z16	nd	nd	nd	nd	nd	nd	256	512	512	512	>512	>512	>256	>256	>256	>64	>64	>64	0.5	0.5	0.5	1	0.5	2	
<i>E. cloacae</i> Z17	nd	nd	nd	nd	nd	nd	0.06	0.125	0.125	0.06	0.125	1	0.5	0.5	1	0.5	1	1	≤ 0.03	≤ 0.03	≤ 0.03	64	64	32	
<i>E. cloacae</i> Z18	nd	nd	nd	nd	nd	nd	0.25	0.25	0.125	0.5	0.5	1	0.5	1	2	2	4	0.06	0.06	0.06	0.5	0.5	0.5		
<i>E. cloacae</i> Z19	nd	nd	nd	nd	nd	nd	256	256	128	512	>512	>512	256	>256	>256	1	2	2	32	32	32	0.5	0.5	1	

Kp, *Klebsiella pneumoniae*; AMC, amoxicillin-clavulanic acid; TZP, piperacillin-tazobactam; CTX, cefotaxime; CRO, ceftriaxone; GEN, gentamicin; AMK, amikacin; LVX, levofloxacin; CST, colistin; nd, not determined. MIC changes by more than one 2-fold dilution in the presence of NAC are shaded.

SUPPLEMENTAL TABLE S2 MICs ($\mu\text{g/ml}$) of antibiotics other than carbapenems, determined in absence and presence of two high NAC concentrations: *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

Antibiotic	CAZ			TOB			AMK			LVX			CST			
	NAC (mM)	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50
<i>P. aeruginosa</i> PAO-1		0.5	0.5	0.5	0.25	0.5	0.5	1	2	2	1	1	1	2	2	2
<i>P. aeruginosa</i> ATCC 27853		1	1	1	0.5	0.5	0.5	2	2	2	1	1	1	2	1	1
<i>P. aeruginosa</i> Z32		8	8	8	0.5	0.5	0.5	1	1	1	2	1	1	0.5	0.5	0.5
<i>P. aeruginosa</i> Z34		128	128	64	32	32	32	16	16	16	8	8	4	2	1	1
<i>P. aeruginosa</i> Z38		1	1	1	0.5	0.5	1	2	4	4	0.125	0.125	0.125	1	1	1
<i>A. baumannii</i> ATCC 17978		nd	nd	nd	nd	nd	nd	2	2	2	0.25	0.25	0.125	1	1	1
<i>A. baumannii</i> RUH 134		nd	nd	nd	nd	nd	nd	4	4	4	0.25	0.25	0.25	1	1	1

CAZ, ceftazidime; TOB, tobramycin; AMK, amikacin; LVX, levofloxacin; CST, colistin; nd, not determined.

SUPPLEMENTAL TABLE S3 MICs ($\mu\text{g/ml}$) of antibiotics determined in absence and presence of two high NAC concentrations: *Moraxella catarrhalis* and *Haemophilus influenzae*

Antibiotic	AMC			CTX			LVX			AZM			SXT			
	NAC (mM)	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50
<i>M. catarrhalis</i> Z72		0.5	0.5	1	0.5	0.5	0.5	0.06	0.06	0.06	0.06	0.06	0.03	nd	nd	nd
<i>M. catarrhalis</i> Z73		0.25	0.25	0.125	0.25	0.25	0.5	0.06	0.06	0.06	0.06	0.03	0.03	nd	nd	nd
<i>H. influenzae</i> ATCC 49247		8	8	8	0.5	0.5	1	0.03	0.03	0.03	nd	nd	nd	0.125	0.125	0.125
<i>H. influenzae</i> Z83		1	2	1	0.125	0.125	0.25	0.015	0.03	0.03	nd	nd	nd	>16	>16	>16

AMC, amoxicillin-clavulanic acid; CTX, cefotaxime; LVX, levofloxacin; AZM, azithromycin; SXT, trimethoprim-sulfamethoxazole; nd, not determined.

SUPPLEMENTAL TABLE S4 MICs ($\mu\text{g/ml}$) of antibiotics other than carbapenems, determined in absence and presence of two high NAC concentrations:

Staphylococcus aureus

Antibiotic	OXA			LVX			SXT			AZM			MIN			VAN			LZD			
	NAC (mM)	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50
<i>S. aureus</i> ATCC 6538		0.125	0.125	0.25	0.125	0.25	0.125	0.125	0.125	0.125	1	1	0.5	0.06	0.06	0.06	1	1	2	2	2	2
<i>S. aureus</i> ATCC 25923		0.25	0.25	0.25	0.25	0.25	0.25	0.125	0.06	0.06	1	1	0.5	0.125	0.125	0.125	2	2	2	2	2	2
<i>S. aureus</i> ATCC 43300		16	16	32	0.25	0.25	0.25	0.125	0.125	0.125	>256	>256	>256	0.06	0.06	0.06	1	1	2	2	2	2
<i>S. aureus</i> MRSA-IT1		8	8	8	8	8	8	0.125	0.125	0.125	2	2	1	0.06	0.06	0.06	2	2	2	4	2	2
<i>S. aureus</i> Z57		0.5	0.5	0.5	0.125	0.125	0.125	0.125	0.125	0.125	1	1	1	0.06	0.06	0.125	1	1	1	4	4	4
<i>S. aureus</i> Z61		0.5	0.5	0.5	0.125	0.125	0.125	0.125	0.125	0.125	2	2	2	0.125	0.125	0.125	2	1	2	4	4	4

OXA, oxacillin; LVX, levofloxacin; SXT, trimethoprim-sulfamethoxazole; AZM, azithromycin; MIN, minocycline; VAN, vancomycin; LZD, linezolid.

SUPPLEMENTAL TABLE S5 MICs ($\mu\text{g/ml}$) of antibiotics determined in absence and presence of two high NAC concentrations: *Streptococcus pyogenes* and *Streptococcus pneumoniae*

Antibiotic	AMX			CRO			LVX			AZM			
	NAC (mM)	0	10	50	0	10	50	0	10	50	0	10	50
<i>S. pyogenes</i> ATCC 12344 ^T		0.03	0.03	0.03	0.03	0.03	0.03	0.5	0.5	0.5	0.125	0.125	0.125
<i>S. pyogenes</i> Z90		≤ 0.008	0.015	0.015	0.015	0.03	0.03	0.5	0.5	0.5	0.125	0.125	0.125
<i>S. pyogenes</i> Z91		0.015	0.03	0.015	0.015	0.03	0.03	0.5	0.5	0.5	0.25	0.125	0.25
<i>S. pneumoniae</i> ATCC 49619		0.06	0.125	0.125	0.125	0.125	0.125	0.5	0.5	0.5	0.06	0.06	0.125
<i>S. pneumoniae</i> Z104		0.015	0.03	0.03	0.03	0.06	0.06	1	1	1	32	32	32
<i>S. pneumoniae</i> Z105		≤ 0.008	≤ 0.008	0.015	0.06	0.06	0.125	1	1	1	32	32	32

AMX, amoxicillin; CRO, ceftriaxone; LVX, levofloxacin; AZM, azithromycin. MICs values were always confirmed by CFU count, required due to the alteration of culture medium (containing 5% lysed horse blood) color in the presence of high NAC concentrations.

SUPPLEMENTAL TABLE S6 MICs ($\mu\text{g/ml}$) of antibiotics other than carbapenems, determined in absence and presence of two high NAC concentrations: *Corynebacterium striatum*

Antibiotic	PEN			AMC			GEN			AZM			VAN			
	NAC (mM)	0	10	50	0	10	50	0	10	50	0	10	50	0	10	50
<i>C. striatum</i> Z114		2	2	0.25	2	2	0.25	8	8	16	>32	>32	>32	0.5	0.5	0.5
<i>C. striatum</i> Z115		32	16	0.5	32	16	1	4	4	8	>32	>32	>32	0.5	0.5	0.5

PEN, penicillin; AMC, amoxicillin-clavulanic acid; GEN, gentamicin; AZM, azithromycin; VAN, vancomycin. MIC changes by more than one 2-fold dilution in the presence of NAC are shaded. MICs values were always confirmed by CFU count, required due to the alteration of culture medium (containing 5% lysed horse blood) color in the presence of high NAC concentrations.

SUPPLEMENTAL TABLE S7 Stability of carbapenems in the presence of NAC.

Compound (experimental conditions)	Antibiotic $t_{1/2}$ (min)		
	Imipenem	Meropenem	Ertapenem
None (PBS, 25°C)	>1000	>1000	>1000
10 mM L-cysteine (PBS, 25°C)	9.5 ± 0.1	10.4 ± 0.1	21.3 ± 0.5
50 mM L-cysteine (PBS, 25°C)	6.3 ± 0.4	3.8 ± 0.1	7.5 ± 0.7
10 mM NAC (PBS, 25°C)	580 ± 9	>1000	>1000
50 mM NAC (PBS, 25°C)	160 ± 2	500 ± 8	>1000
None (PBS, 37°C)	>1000	>1000	>1000
10 mM NAC (PBS, 37°C)	550 ± 30	>1000	>1000
50 mM NAC (PBS, 37°C)	66 ± 5	220 ± 30	530 ± 40
None (CAMHB, 37°C)	>1000	>1000	>1000
10 mM NAC (CAMHB, 37°C)	200 ± 40	670 ± 160	>1000
50 mM NAC (CAMHB, 37°C)	52 ± 6	145 ± 15	225 ± 20

The half-life ($t_{1/2}$) of antibiotics was computed from the pseudo-first order rate constant for carbapenem beta-lactam ring opening, measured by following the time-dependence variation of absorbance at 300 nm (values are the mean of four independent experiments), followed in both PBS buffer and in cation-adjusted Mueller-Hinton Broth (CAMHB) and at 25 or 37 °C. L-cysteine was tested as a comparator in experiments performed at 25°C in PBS.